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(54) **PREPARATION BIOSYNTHETIQUE EN POUDRE PRODUITE A
PARTIR DE BOIS DE CERFS OSSIFIES ET ADDITIF
ALIMENTAIRE A BASE DE CETTE PREPARATION**

(54) **POWDERY BIOGENIC PREPARATION FROM OSSIFIED DEER
ANTLERS AND A FOOD ADDITIVE BASED ON SAID
BIOGENIC PREPARATION**

(57) Préparation biosynthétique produite à partir de bois de cerfs ossifiés, ayant l'aspect d'un produit broyé brut d'une taille granulométrique inférieure à 0,16 mm, d'une surface spécifique d'environ 100 m carrés/g et d'une porosité d'environ 3,0 m carrés/g. L'additif alimentaire contient, comme agent biologique actif, la préparation biosynthétique en poudre produite à partir de bois de cerfs ossifiés.

(57) The biogenic preparation from ossified deer antlers appears as a disintegrated initial product having the particle size below 0.16 mm, a specific surface of about 100 sq.m/g, and a pore volume of about 3.0 cu.m/g. The food additive contains as a biologically potent product the powdery biogenic preparation from ossified deer antlers.

ABSTRACT OF THE SPECIFICATION:

POWDERY BIOGENIC PREPARATION FROM OSSIFIED DEER ANTLERS
AND A FOOD ADDITIVE BASED ON SAID BIOGENIC PREPARATION

The biogenic preparation from ossified deer antlers appears as a disintegrated initial product having the particle size below 0.16 mm, a specific surface of about 100 sq.m/g, and a pore volume of about 3.0 cu.m/g.

The food additive contains as a biologically potent product the powdery biogenic preparation from ossified deer antlers.

POWDERY BIOGENIC PREPARATION FROM OSSIFIED DEER ANTLERS
AND A FOOD ADDITIVE BASED ON SAID BIOGENIC PREPARATION

Field of the Invention

The invention relates in general to curative and nutritive biologically active products, and more specifically it concerns a powdery biogenic preparation from ossified deer antlers and a food additive based on said biogenic preparation.

10 The invention can find application in producing medicinal agents, foodstuffs enriched with biologically potent substances, and can also be used in cosmetics, as well as in fodder production.

Background of the Invention

Known in the art are animal-origin biogenic

preparations successfully applicable in medical and veterinary practice, pantocrine and rantarine being the most widely recognized preparations obtained from deer antlers.

5 For instance, pantocrine which is essentially a 10% alcoholic extract of antlers of deer (that is, Siberian stag, Manchurian deer, and sika deer) contains a great deal of biologically-active substances that provide for a broad range of indications for its application (SU, A,
10 195,049). Pantocrine has the following chemical composition:

	organic substances	75	wt. %
	inorganic substances	25	wt. %,
	wherein:		
15	total nitrogen	8.4	wt. %
	protein nitrogen	8.3	wt. %
	nonprotein nitrogen	0.15	wt. %
	proteins	52.7	wt. %
	lipids	5.6	wt. %
20	mono- and disaccharides	15.5	wt. %
	ash	25.0	wt. %.

In addition, pantocrine contains a great proportion of macroand microelements (Ca, Na, Ag, Cu, Ti, Al, Fe, Si, Mg, Pb, P) among which Fe dominates. A principal
25 part of the active principle of pantocrine is the lipoid fraction, while the biogenous bases, that is, choline

and ethanolamine are the predominant phospholipids. Studies of pantocrine demonstrated a considerable proportion of cholesterol, steroids (estrone, testosterone, progesterone, cholesterol ethers with
5 oleic, stearic, and butyric acids).

It is noteworthy that as little as one half of lipids is transferred from antlers to pantocrine, and a ratio between their fractions is somewhat different. In addition, deer antlers feature a higher content of
10 phospholipids and sterol ethers. The ratio between the lipids of different classes in pantocrine varies depending on extracting conditions.

The preparation rantarine is a liquid extract (1:1) from antlers of males of reindeer obtained by
15 repercolation on 40% ethanol (cf. a textbook "Rantarine" by I.I.Brekhman, Moscow, Vneshtorgizdat PH, 1978 (in Russian). As is evidenced by studies performed, raindeer antlers differ from those of sika deer only in the amount of saccharides which is twice as large. (13.4
20 wt.%) in reindeer antlers. That is why rantorine and pantocrine are principally similar as to chemical composition, that of rantorine being as follows:

Essential amino acids, mg/l:

	arginine	0.404
25	valine	0.823

	histidine	0.078
	isoleucine	0.340
	leucine	0.831
	lysine	0.505
5	methionine	0.080
	threonine	0.142
	phenylalanine	0.616
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	Total	3.319 mg/l
10	Elements, mcm/ml:	
	calcium	53.93
	potassium	2588.4
	sodium	3019.4
	magnesium	34.5
15	iron	2.17
	copper	1.73
	zinc	0.65
	manganese	0.02
	nickel	0.02
20	chromium	0.02
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	Total	5701.2 mcm/ml

The aforementioned animal-origin medicinal preparations have found widespread use as physiological

stimulators, in disorders of the nervous system, dysmetabolism, atherosclerosis, hypotension, and sexual impotence.

Both rantarine and pantocrine are dispensed not only as alcoholic extracts but also as tablets, wherein
5 said extract serves as the active principle.

The potency of antler extracts is to a great extent influenced by the preservation techniques of antlers, as well as by the extraction procedure. It is during preservation of antlers and extraction of pantocrine
10 therefrom that the valuable components of the initial product, that is, proteins, peptides, and blood elements are subject to destruction to a considerable extent. On the other hand, unpreserved antlers can be stored for as little as 6-10 hours after cutting-off, or within 10
15 days at minus 4°C.

Furthermore, the generally adopted antler extraction techniques fail to provide a complete isolation of pharmacologically valuable substances, otherwise speaking, all the preparations obtained from
20 deer antlers known currently are depleted in ingredients compared with the initial product. Thus, it has been found that more than 90% of a total content of valuable and biologically-active antler components remains in the waste product of the production process, that is, in the
25 residues.

Apart from the aforesaid, the abovementioned

biogenic preparations possess a pronounced side effect, consisting in hemolytic and allergenic properties which is due to a considerable content of proteins and peptides, many of them being toxic. A large cholesterol
5 content remaining in the finished product, is causative of atherosclerosis, lipoid hyperplasia, and other diseases stemming from an excess amount of cholesterol in human organism.

Known in the art are nutritional additives
10 (nutriceutics, naturopathic agents) containing biologically-active products in the form of concentrates of natural biologically-active substances or those identical thereto obtained from processing vegetable or animal raw stock, as well as by chemical or
15 biotechnological methods using traditional, nontraditional, or special techniques and adapted for direct intake along with food or for being introduced into specialized food products with a view to enriching the ration with individual nutrients and/or biologically
20 active substances, or with their complex.

The aforementioned nutritional additives are produced in the form of extracts, fusions, balms, isolates, powders, dry and liquid concentrates, syrups, tonics, tablets, or capsules. The problem of elaborating
25 and applying nutritional additives enhancing resistance of human organism to harmful effects of the surrounding medium becomes still more urgent in the regions with

unfavorable ecological situation.

Summary of the Invention

It is an object of the present invention to provide a powdery biogenic preparation from a readily available
5 animal raw material which is better balanced, as to its composition, to human organism.

It is another object of the present invention to provide such a food additive based on animal raw material that allows of sanitation of human organism and
10 increasing its adaptogenic resources, as well as avoiding any side effect thereof.

The foregoing objects are accomplished due to the provision of a novel powdery biogenic preparation from ossified deer antlers which consists of porous particles
15 of a disintegrated initial product, the dispersity of said particles being largely below 0.25 mm, their specific surface about 100 sq.m/g, and a volume of pores of about 3.0 cu.m/g.

The proposed invention is instrumental in the
20 provision of a biogenic preparation with a retained natural potency of the initial product and possessing a high specific adsorptive activity, antacid, and enveloping properties, as well as a broad range of pharmacological action.

25 A variant of protection afforded by the present

invention is a powdery biogenic preparation containing substantially as follows:

	lipids	0.13-0.25 wt. %
	essential amino acids and peptides,	
5	not less than	0.80 mg/g
	cholesterol	0.10-0.20 mg/g
	phosphorus, not less than	3.5 wt. %
	calcium	15.0-20.0 wt. %
	iodine	0.02-0.04 wt. %
10	magnesium, not more than	6800.0 mcg/g
	barium, not more than	1.30 mcg/g
	manganese, nor more than	3.5 mcg/g
	tin	0.50 mcg/g
	copper	0.5-20.0 mcg/g
15	iron	60-240 mcg/g
	zinc	60-120 mcg/g
	lead, less than	0.35 mcg/g
	cadmium, less than	0.001mcg/g
	cesium	4-12 mcg/g
20	strontium	5-10 mcg/g
	potassium	300-600 mcg/g.

The present invention is instrumental in producing a biogenic preparation from ossified antlers of raindeer, wherein macroand microelements are in a ratio
25 and amounts most completely meeting the physiological demand of human organism, said preparation having in this respect high adaptogenic activity, as well as

immunostimulating and immunomodeling properties.

The herein-proposed biogenic preparation contributes, due to its composition, to a better activity of the cardiac muscles and promotes blood
5 coagulation processes.

Another subject-matter of protection is a food additive containing a biologically potent active product which, according to the invention, is in fact a powdery biogenic preparation from ossified deer antlers, the
10 porous particles of said preparation featuring a dispersity principally below 0.25 mm, a specific surface of about 100 sq.m/g, and a pore volume of about 3.0 cu.m/g; it is expedient, according to the invention that said biogenic preparation be principally of the
15 following composition:

	lipids	0.13-0.25 wt.%
	essential amino acids and peptides,	
	not less than	0.80 mg/g
	cholesterol	0.10-0.20 mg/g
20	phosphorus, not less than	3.5 wt.%
	calcium	15.0-20.0 wt.%
	iodine	0.02-0.04 wt.%
	magnesium, not more than	6800 mcg/g
	barium, not more than	31.30 mcg/g
25	manganese, nor more than	3.5 mcg/g
	tin	0.50 mcg/g
	copper	0.5-20.0 mcg/g

	iron	60-240	mcg/g
	zinc	60-120	mcg/g
	lead, less than	0.35	mcg/g
	cadmium, less than	0.001	mcg/g
5	cesium	4-12	mcg/g
	strontium	5-10	mcg/g
	potassium	300-600	mcg/g.

The herein-proposed food additive makes possible both prevention and treatment of the aforementioned diseases. Thus, said food additive is capable of increasing human adaptogenic resources, normalizing the metabolic effect, enhancing immunobiologic potencies and defenses of human organism, and stimulating taking heavy metals and toxins out of human organism.

Further objects and many of the attendant advantages of the present invention will be readily appreciated as the same becomes better understood by reference to the following detailed description of a novel powdery biogenic preparation, a food additive based on said preparation, experimental and clinical trials of the proposed biogenic preparation and of said food additive based thereon.

Description of a Preferred Embodiment

The herein-proposed novel biogenic preparation appearing as a powdery product wherein approximately 80%

of porous particles thereof feature a dispersity below 0.25 mm, a specific surface of about 100 sq.m/g, and a pore volume of about 3.0 cu.m/g, has been produced from ossified deer antlers, that is, Siberian stag, 5 Manchurian deer, sika deer, reindeer, moose, and European stag.

The novel biogenic preparation appears as a grey-colored loose powder having inclusions of light-brown particles, has a specific nonputrescent 10 odor, and is virtually insoluble in water and organic solvents.

The weight percent of volatiles therein is as low as 13.0, and that of total ash is as low as 49.5. Biological potency of the proposed preparation stems 15 from the initial product.

A sample analysis of a batch of the proposed powdery biogenic preparation carried out by thin-layer, gas-liquid, highefficiency chromatography, UF-spectrophotometry, elementary analysis for C, H, N, 20 S, and I, as well as chromatomass-spectrometry, polarimetry, titrometry, and gravimetry has found the following chemical composition of said preparation:

	Carbon	20.0 wt.%
	Nitrogen	6.5 wt.%
25	Sulfur	< 0.1 wt.%
	Hydrogen	3.5 wt.%
	Phosphorus	4.2 wt.%
	Iodine	0.012wt.%

	Calcium	174,940	mg/kg
	Sodium	4,260	mg/kg
	Potassium	582	mg/kg
	Magnesium	6,643	mg/kg
5	Iron	77	mg/kg
	Zinc	95.5	mg/kg
	Copper	0.66	mg/kg
	Manganese	3.5	mg/kg
	Chromium	0.22	mg/kg
10	Nickel	0.52	mg/kg
	Cobalt	0.04	mg/kg
	Lithium	0.9	mg/kg
	Rubidium	3.4	mg/kg
	Cesium	4.4	mg/kg
15	Barium	31.3	mg/kg
	Strontium	8.6	mg/kg
	Molybdenum	1.6	mg/kg
	Lead	0.32	mg/kg
	Cadmium	< 0.001mg/kg	
20	Arsenic	0.15	mg/kg
	Mercury	< 0.005mg/kg	
	Tin	0.50	mg/kg.

It is worth noting that analyses of the various
samples of the proposed preparation may give slightly
25 different results.

The herein-proposed powdery biogenic preparation

from ossified reindeer antlers contains principally as follows:

	lipids	0.13-0.25 wt. %
	essential amino acids and peptides,	
5	not less than	0.80 mg/g
	cholesterol	0.10-0.20 mg/g
	phosphorus, not less than	3.5 wt. %
	calcium	15.0-20.0 wt. %
	iodine	0.02-0.04 wt. %
10	magnesium, not more than	6800 mcg/g
	barium, not more than	31.30 mcg/g
	manganese, nor more than	3.5 mcg/g
	tin	0.50 mcg/g
	copper	0.5-20.0 mcg/g
15	iron	60-240 mcg/g
	zinc	60-120 mcg/g
	lead, less than	0.35 mcg/g
	cadmium, less than	0.001mcg/g
	cesium	4-12 mcg/g
20	strontium	5-10 mcg/g
	potassium	300-600 mcg/g.

The fact that the proposed powdery biogenic preparation from reindeer antlers contains a combination of a large amount of biologically potent compounds and
 25 micro- and macroelements in a physiological ratio optimum for human organism, as well as its specific adsorptive activity are responsive for its ability to

regulate metabolic and redox processes, hemopoiesis, functions of endocrine glands. The preparation is also capable of increasing immunological status of the organism, stimulating the growth and development of the bone and muscular tissues, and bringing heavy metals and toxins out of human organism.

Complex studies into the chemical composition and physical properties of the powdery biogenic preparation from ossified deer antlers, as well as its preclinical trials have demonstrated that a great amount of active elements, such as calcium and magnesium, and barium which are the principal components of the osseous tissue, stimulates its growth and development, and also provides for a better activity of the cardiac muscles and promotes blood coagulation processes.

The proposed preparation features the content of steroid compounds, including those producing hormonal effect (estrogens, androgens, progesterone) one order of magnitude lower than the known preparations from deer antlers; furthermore, the proposed preparation contains the amount of cholesterol causative of atherosclerosis, lipid hyperplasia, and other diseases, ten to fifteen times lower than the known preparations.

For instance, the iodine content in the form of iodated derivatives of amino acid tyrosine (tyronine, thyroxin, 3,5-diiodotyrosine, 3,5,3'-triiodotyronine, 3,3'-diiodotyronine) in an amount exceeding 0.02 wt.%

ensures a normal activity of the endocrine system of human organism, including the thyroid gland which influences the protein and lipid metabolism.

A great content of manganese is important for
5 activating the redox processes in human organism.

The proposed preparation contains a little amount of proteins and peptides many of which may be toxic or possess hemolytic and allergenic properties. In addition, it contains a great proportion of phosphorus
10 which is extremely necessary for promoting the growth of the bone tissue and for normal functioning of the nervous system, as well as is indicated in vascular hypotension, rachitis, and diatheses.

The herein-proposed biogenic preparation from
15 ossified deer antlers possesses antacid, adsorptive, and enveloping properties and exhibits also an acid-basic capacity which is important when using the preparation in treating peptic ulcer of the stomach and duodenum, gastritis, heartburn, gastrointestinal pain, and other
20 gastro- and enteropathies, in which reduced acidity and proteolytic activity of the gastric juice is indicated.

The amount of heavy toxic metals (lead, cadmium, mercury, molybdenum, cobalt, and other) is within permissible ranges which do not exceed the established
25 norms that rule out accumulation of toxic metals in human organism.

The evidences we have obtained are indicative of

the fact that there is no substantial difference, as to chemical composition, between the powdery biogenic preparations produced from ossified antlers of deers of different species, that is, Siberian stag, Manchurian deer, sika deer, or reindeer.

The attained physicochemical and organoleptic quality characteristics of the proposed powdery biogenic preparation from ossified deer antlers, including microbiological characteristics and content of heavy metals, provoke no objections from the hygienic standpoints.

Pharmacological and toxicological studies of the proposed powdery biogenic preparation from ossified deer antlers have been performed on animals of different species, i.e., albino mice, rabbits, guinea pigs, using different doses of the preparation, the trialed ones inclusive. It has been found that the proposed preparation exhibits no acute toxicity: the doses 15-210 times (for mice) and 9-90 times (for rabbits) higher than the recommended produce no toxic effect. Nor have its toxic properties been detected in chronic experiment on rabbits administered 160 mg/kg of the preparation for a month. No changes have been observed in: weight of animals, relative weight of their viscera, a number of biochemical characteristics (total protein, albumin, globulin, creatinine, glucose), morphological characteristics of the internal organs, and

hematological characteristics of the peripheral blood. Chronic experiment on mice given daily doses of the preparation, according to the invention, in an amount of 225 mg/kg and 1225 mg/kg has detected no changes in the
5 relative weight of the internal organs and in their morphology. The proposed powdery biogenic preparation produces no local irritant effect. No signs of allergic reaction have been observed when studying an allergenic action of the preparation in a dose 70 times the
10 recommended one. The proposed preparation were administered to guinea pigs orally in a dose of 1 g/kg three times a day; in 21 days a skin reaction was observed after applying an electuary of the proposed preparation to skin. In addition, the preparation is not
15 cytogenetically active when administered in doses of 1300 and 7800 mg/kg (the dose six times the recommended one). When given in a dose of 1300 mg/kg the preparation produces an antimutagenic action.

Studies into the pharmacological properties of the
20 proposed powdery biogenic preparation have detected as follows: the preparation reduces arterial blood pressure (by 13% on the average) in rabbits, stimulates the development of the genitalia (experiments were carried out on sexually immature albino mice given the
25 preparation in different doses, the best result being obtained with a dose of a 5% physiological saline). There are noticed an increase in the relative weight of

the genitalia, a higher RNA content of the prostate epithelium (in the cytoplasm), and hypertrophy of the secretory elements, and hypertrophy of the cells of the seminal vesicles. The powdery biogenic preparation from
5 ossified deer antlers possesses hepatoprotective and lipotropic action, produces an effect on the immune system, and stimulates the lymphatic follicles of the spleen. There is also established an effect produced by the proposed preparation on the intensity of oxygen
10 absorption by cells in experiments in vitro. High doses of the preparation inhibit, and low doses stimulate oxygen absorption by cells. In addition, the proposed preparation has an adsorptive capacity and is therefore effective against food poisoning.

15 The powdery biogenic preparation proposed herein has been studied in a number of specialized therapeutic institutes, where its positive effect has been established. Thus, it has been found in the Institute of experimental endocrinology (Moscow, Russia) that the
20 proposed preparation causes no negative shifts in the analyzed characteristics of the condition of the endocrine system and metabolism in test rats. The slight changes revealed are indicative of a general growth-stimulating effect produced by the preparation.
25 Presence of iodine in the preparation imparts a protective effect of the preparation on the thyroid gland in cases of its possible radiation injuries.

It has been found in the Central Institute of Traumatology and Orthopedics Research (Moscow, Russia) that use of the preparation on a simulation of bone fracture in experimental animals (rabbits) results in an earlier and more complete formation of a callus compared with control animals and causes no pathologic changes in the bone tissue. Use of the preparation in an experiment (bone-muscle injury) reduces inflammatory, dystrophic and microcirculatory changes, thus reducing secondary necrotizing of muscular tissue and promotes filling of the wound canal with maturing granulation tissue. The healing period of skin-muscle wounds is cut down nearly twofold compared with the control.

Experiments conducted in the Urology Research Institute (Moscow, Russia) enable one to infer that the preparation is capable of stimulating the functional capabilities of the kidneys and of the organs of the male reproductive system, it adds to resistance of tissues and cells to the effect of disturbing factors, in particular, microorganisms and their toxins.

Trialing of the proposed preparation on experimental tuberculosis in inbred mice has demonstrated that the preparation produces a positive effect on tissue reactions in cases of tuberculous inflammation in experimental animals infected with *Mycobacterium tuberculosis* H37Rv, thus contributing to their survival. As evidenced by histologic studies, the

proposed preparation is found to produce an inhibitory effect on the development of specific inflammation in the organs of experimental animals, starting from the initial stages of infection (8 days) and stimulates
5 proliferation of lymphocytes not only in the immunocompetent organs, such as the spleen but also in target organs, that is, the lungs and the liver, affected with tuberculosis.

A positive effect of the preparation on tuberculous
10 inflammation is especially conspicuous when used in complex therapy of tuberculosis along with antibacterial drugs, and is most pronounced in the late period of the disease's (18 days). In this case a more complete resolution of tuberculous foci in the lungs, liver, and
15 spleen.

Thus, the studies carried out have demonstrated that the proposed preparation possesses some immunomodulating action which tells positively on resistance offered by test mice to tuberculosis
20 infection.

Studies into the effect produced by the proposed preparation on the peripheral blood and bone marrow composition, erythrograms, and some of the biochemical characteristics of blood in rats give evidence that:

- 25 1. The general status (weight, behavioral reactions, rate of food and water consumption, the condition of the gastrointestinal tract) in animals

given the preparation in doses of 7 and 13 mg differ in nothing from the similar characteristics in control animals.

2. The preparation administered to intact test rats
5 in the experimental doses causes no changes whatever in the amount of erythrocytes, hemoglobin, hematocrit value, and in the erythroid offshoot of the bone marrow.

3. Resistance of the peripheral blood erythrocytes to the effect of a chemical hemolytic agent increases
10 irrespective of the dose of the preparation.

4. When taken in both of the aforementioned doses the preparation contributes to a substantial increase in the amount of thrombocytes in the peripheral blood and to fibrinogen concentration in intact animals even
15 concurrently with blood loss.

5. Intact animals administered the preparation exhibit a reduced absolute number of lymphoid elements in both peripheral blood and bone marrow.

6. When administered in both doses against a
20 background of chronic blood loss the preparation contributes to restoration of the bone marrow erythroid offshoot and the red blood quotients under study. Acid resistance of erythrocytes in blood-loss animals increases to a greater extent than in intact animals,
25 this effect being dose-dependent.

7. Administration of the preparation to test animals against a background of blood loss contributes

to restoration of the bone marrow granulocytic offshoot and of the peripheral blood polynuclear hemocytes.

Studies into the effect of the proposed biogenic preparation on experimental peptic ulcer of the stomach
5 in test rats have demonstrated that the reparation processes in the animals given the proposed preparation proceed faster than in the control animals and the reparation period is by 2 or 3 days shorter.

Studies into the effect of the proposed biogenic
10 preparation on the development of a pathologic process in the pancreatic tissue in experimental pancreatitis have demonstrated as follows.

1. The preparation is capable of inhibiting a pathologic process in the pancreatic tissue in early
15 stages of experimental pancreatitis. This effect is especially clear cut in macroscopic examination (less pronounced edema of the pancreas and of the surrounding tissues, the symptoms of adhesive peritonitis are nearly absent).

20 2. The preparation stimulates the development of the process of reorganization in the pancreatic tissue which is evidenced by a more pronounced symptoms of same in the animals of the experimental group.

The preparation has been assessed for biological
25 potency on a short-term culture of human epidermic cells, the following findings being obtained.

The preparation is but slightly soluble in water,

nontoxic to human epidermic cells whose adhesive properties increase with a reduction of the preparation dose. The preparation has a markedly pronounced proliferative effect, the proliferative response
5 increasing with a reduction of the preparation dose. Thus, a dose of 0.1 mcg/ml increases DNA synthesis threefold, a dose of 1 mcg/ml, twofold, and a dose of 5 mcg/ml, by 50 percent, whereas the doses of 10 and 50 mcg/ml produce no effect whatever on the proliferative
10 response. The dose-dependent effect of an increase in protein synthesis is the same as in the proliferative response; thus, a dose of 0.1 mcg/ml has been found to increase the protein synthesis 3.5 to 4 times.

When administered in doses of 0.1 to 0.001 mkg/ml
15 the preparation produces no effect on expression of human histocompatibility antigens.

The proposed food additive has been tested, in the Nutrition Research Institute under the Academy of Medical Sciences of the Russian Federation (Moscow), for
20 a number of toxic elements, calcium, and phosphorus. Test samples were prepared in compliance with the norms prescribed in the USSR State Standard GOST 26927-86 entitled "Edible raw materials and foodstuffs. Mineralization for determining toxic elements". Tests
25 for lead, cadmium, zinc, copper, and calcium were conducted in keeping with the methodological instructions on atomic-adsorption techniques of

determining toxic elements in foodstuffs and edible raw materials. The maximum content of said toxic elements has been found to be 0.001 mg/kg. The arsenic content of the proposed food additive was determined colorimetrically to be 0.1 mg/kg. The inorganic phosphorus content was determined spectrophotometrically.

The examination findings are tabulated in Table 1.

Table 1.

10	Name of elements	Content, mg/kg
	1. Lead	0.75
	2. Cadmium	0.030
	3. Arsenic	0.11
	4. Zinc	89.1
15	5. Copper	2.23
	6. Phosphorus, %	9.7
	7. Calcium, %	23.0

The proposed food additive has been trialed in the clinic of dietotherapy of the Nutrition Research Institute under the Academy of Medical Sciences of the Russian Federation in the controlled hospital conditions on patients with cardiovascular pathology and

concomitant adiposity, using a broad range of biochemical tests characteristic of the lipid, carbohydrate, and protein metabolism, the immunological status and the condition of patients' antioxidant protection. The findings obtained enable one to state as follows.

- The answers given to a questionnaire by the patients suffering from hypertensive disease with concomitant adiposity demonstrate that ingestion of the proposed food additive concurrently with a reduced-caloricity hyposodium anti-atherosclerosis diet contributes to suppression of the sensation of hunger in a majority of patients. In this case, no symptoms of intolerance to said nutraceutic nor allergic reactions are observed.

- The degree of body weight loss expressed in percent of the body weight prior to the treatment and attained in the course of dietotherapy using the Ar ration and the proposed food additive, exceeds by 50% that attained when using the diet alone, which is seemingly due to a reduced sensation of hunger the resultant psychological comfort.

- Enrichment of the hypocaloric hyposodium diet with the proposed nutraceutic promotes the hypotensive effect of the ration, which is pronounced to the greatest extent with respect to systolic arterial pressure.

- Use of the food additive under trial contributes to a considerably reduced abdominal discomfort in patients suffering from biliary and colic dyskinesia. In the course of treatment these patients exhibited reduced
5 meteorism, dyspeptic phenomena, and abdominal pain.

- The most substantial positive changes in the biochemical characteristics, especially pronounced in patients with concomitant hyperlipoproteinemia and attained due to enrichment of the antiatherosclerosis
10 diet with the proposed food additive, are observed with respect to cholesterol whose level in the blood serum is reduced about twofold compared with the control.

- Incorporation of the proposed food additive in the Ar diet renders a positive effect on the
15 carbohydrate and protein metabolism, the functional state of the liver, and the characteristics of the blood coagulation and anticoagulation systems.

- An analysis of the changes in characteristics indicative of the condition of the system "peroxidation
20 of lipids" - antioxidant protection - enables one to infer that the proposed food additive produces a favorable effect on the antioxidant status of the organism and on the metabolism of lipids, thus promoting a reliable reduction in the concentration of the primary
25 and secondary products of peroxidation of lipids in the course of treatment.

- It is due to the use of the dietotherapy

incorporating the proposed food additive that an immunomodulating effect of said nutraceutic is revealed, which manifests itself by a reliable increase in production of immunoglobulins A and C, within the norm
5 limits, by about one-third compared with their level before treatment.

The recommended daily dose of the proposed food additive is 400 ml/day before taking meals (breakfast or dinner) and is to be washed down with 100 ml water. A
10 total duration of the treatment course is one month. A treatment course can be repeated two or three times a year.

According to evidence of functional, histologic, and morphometric examinations, the proposed biogenic
15 preparation produces an effect of two kinds when used in an acute infectious morbid process. On the one hand, it prevents tissue destruction in case of an acute purulent inflammation, and on the other hand, it stimulates the system of lymphomacrophagocytes, which is
20 morphologically demonstrated in an increased amount of lymphoid follicles and a larger area thereof. A lesser extent of tissue destruction results in a better functional intactness of the kidneys and in restoration of all characteristics deranged due to the inflammatory
25 process.

The experiments conducted allow one to infer that the proposed preparation is capable of stimulating the

functional capabilities of the kidneys and the male reproductive organs. Moreover, resistance of tissues and cells to the effect of disturbing factors, in particular, microbial agents and their toxins, is increased due to nonspecific stimulation of the defense mechanisms, whereby the function of the affected organs is impaired to a less extent and normalizes more quickly.

A total of 20 patients (8 males and 12 females) aged from 36 to 58 and suffering from hypertensive disease of stage I-II with concomitant stage I-II adiposity were observed under controlled hospital conditions. The patients of the control group (10 persons) were given a caloricity-reduced hyposodium, hypolipidemic antiatherosclerosis diet Ar, an energy (caloric) value of the ration being 1500 kcal. 10 patients of the experimental group were instituted the same diet for the same period, and additionally they took 400 ml of the proposed preparation daily in the morning or the day-time before meals and washed the preparation with 100 ml water.

The patients of the experimental and control groups were identical as to the nature and degree of severity of the principal disease (that is, stage I-II hypertensive disease), the concomitant pathology (hyperlipoproteinemia of a primary and secondary genesis, biliary and colic dyskinesia, deforming

spondylosis and osteochondrosis of the cervicothoracic and lumbar spine), and the sex and age characteristics. An excess body weight not exceeding 30% was noted in 25% of the patients in both experimental and control groups.

5 It is no mere chance that the patients with stage I-II hypertensive disease and concomitant adiposity, as well as those with concomitant hyperlipoproteinemia were selected as the object of observation in the aforesaid clinical trials. The presence of absorptive and
10 adaptogenic properties in the food additive under trial is directly linked with the pathogenetic mechanisms of affection of the cardiovascular system in the patients under observation and, in particular, with lipid dysmetabolism, modified immune reactions, and disturbed
15 interrelations in the system "peroxidation of lipids - antioxidant organism protection".

Characteristics of the Ar diet used.

The chemical composition and energy (calorific) value of the Ar diet used are presented in Table 2.

20

Table 2

Chemical composition and energy value of Ar diet

Characteristics	Quantity
Proteins, g	75.0
including animal ones	45.0

	Fats, g	70.0
	including vegetable ones	25.0
	Carbohydrates, g	190.0
	including simple ones	15.0
5	Caloricity, kcal	1690.0
	Vitamins:	
	B1, mg	0.75
	B2, mg	1.46
	B6, mg	1.57
10	C, mg	92.0
	PP, mg niac.eq.	11.6
	E, mg toc.eq.	3.25
	A, mcg ret.eq.	200.0
	beta-carotin, mg	4.3
15	Mineral substances, g:	
	sodium	1.8
	potassium	4.0
	calcium	0.8
	magnesium	0.6
20	phosphorus	1.2

Table 3

Generalized amounts of losses due to heat treatment

Food	B1	B2	C	PP	A	beta-	Ca	Mg	P
additive						carotin			

Percent									
of loss	28	20	60	20	40	20	12	13	19

Hyposodium caloricity-reduced antiatherosclerosis diet Ar is featured by a reduced amount of animal fats and oligosaccharides, as well as by a physiological norm of protein, restriction as to cholesterol-containing foods and extractive substances, and enriching the ration with foods containing lipotropic substances, polyunsaturated fatty acids, and edible fibers. The mineral composition is balanced adequately to the pathogenetic essence of the coronary heart disease and the hypertensive disease.

A complex examination of the patients included studying the changes in the objective signs of the disease, body weight, arterial pressure, a biochemical examination performed with the aid of the model "Spectrum" analyzer available from Abbot Co., USA, using a standard set of reagents and a standard programme.

Lipoid metabolism was assessed against a concentration of total cholesterol and triglycerides in blood.

In order to assess protein metabolism, total protein of the blood serum and uric acid were determined, while carbohydrate metabolism was assessed

by determining glucose.

The functional capability of the liver was assessed against the content of total bilirubin, AST and ALT in blood serum. The condition of the coagulation and
5 anticoagulation blood systems was judged against the Quick's prothrombin consumption index, fibrinogen was determined by the Rutberg's technique, and blood fibrinolytic activity, by the Kowalski, Kopek, and Niverski technique.

10 The condition of the system of antioxidant protection and of peroxidation of lipids was assessed by measuring the following characteristics in erythrocyte hemolysates:

- Activity of superoxide dismutase (SOD) was
15 determined using a classical technique according to Beauchamp C., Fridovich J., 1971.

- Activity of glutathione peroxidase (GP) was assessed using the method of Mille G., 1959 in modification for the automatic analyzer
20 "Clinicon-Korona" available from the firm LKB, Sweden.

- Activity of glutathione reductase (GR) was determined on the basis of a classical technique of Tilbotson J.A. et al., 1971 in modification for the automatic analyzer "Clinicon-Korona" available from the
25 firm LKB, Sweden.

- Activity of catalase was determined by the technique developed and modified for the automatic

analyzer "Clinicon-Korona".

- Content of diene conjugates was determined by the method of I.D.Stalnaya and T.G.Garishvili, 1977 in modification for erythrocytes.

5 The following components of nonenzymatic antioxidant protection were determined:

- SH-groups in blood serum, using Ellman's spectrophotometric technique.

- Concentration of vitamins A and E in blood serum
10 was determined by the fluorimetric technique of R.I.Cherliauskene, 1984, that of vitamin C, by titration.

Concentration of immunoglobulins A, G, and M and of the components of complements C3 and C4 was determined
15 by an immunochemical technique, using the model "ICS-II" analyzer available from Beckman, USA.

All examinations were conducted dynamically so as to assess the effects of the performed alimentary intervention.

20 No symptoms of intolerance of the proposed food additive nor any allergic reactions were noticed in the course of day-to-day clinical observation of the patients during clinical trials.

Contrariwise, the patients suffering from biliary
25 and colic dyskinesia who were given the proposed food additive, exhibited reduced meteorism, dyspeptic phenomena, and abdominal pain. A majority of the

patients noted a reduced sensation of hunger.

With a view to revealing a lipolytic effect of the food additive under trial, there was performed a comparative analysis of the degree of body weight loss in the patients given the proposed food additive concurrently with the antiatherosclerosis diet and in the patients of the control group who were instituted the basic diet alone. A total body weight loss in the patients administered the proposed nutriceutic was found to exceed that in the control patients, that is, an average loss of weight in the experimental group was 6.4% of its level prior to treatment, whereas that in the control group equalled 5.2%. An average daily loss of body weight in the patients of the experimental and control groups was 305 g and 247 g, respectively.

Adding the proposed food additive to the ration promoted the hypotensive effect of said ration. Thus, for instance, in the course of the dietotherapy the level of the systolic arterial pressure in the patients of the experimental and control groups was reduced by 31% and 24%, and that of the diastolic pressure, by 19% and 15%, respectively, compared with the figures before the treatment.

When studying the effect of the proposed food additive on biochemical indices, attention is attracted by the pronounced changes in the level of total cholesterol in blood serum. Thus, in the course of the

dietotherapy a hypocholesterolemic effect in the patients of the experimental group was equal to 20% of the initial level, while that in the patients of the control group was 9%. The level of triglycerides in blood serum remained virtually unaffected as a result of treatment, being in the limits of normal variation in the patients of both groups. A hypoglycemic effect in said patients was found to be approximately the same as well.

Changes in the level of total protein in blood serum were insignificant, and the blood uric acid content reduced reliably in the patients of both groups approximately at the same rate. There was also noticed a considerable reduction the blood level of AST and ALT, as well a moderate decrease in the total bilirubin content in the patients given the proposed food additives concurrently with the Ar diet (see Table 4).

Reduction of the prothrombin consumption index in the course of dietotherapy was twice as more pronounced in the patients of the experimental group, whereas a favorable change in the fibrinogen level and fibrinolytic activity of blood was the same in the patients of both groups.

When assessing the effect of the proposed food additive on provision with vitamins there was established a noticeable increase in the concentration of vitamins A and E in the blood of the patients being

treated, whereas no such an effect was observed in the patients of the control group (see Table 5).

Use of the proposed food additive concurrently with the reduced Ar diet contributed also to improvement of some characteristics and activation of the enzymatic antioxidant protection. Thus, for example, in the course of treatment the patients of the experimental group suffering from hypertensive disease and adiposity exhibited a reliable increase in the level of glutathione peroxidase and superoxide dismutase of erythrocytes, whereas such an increase was pronounced to a much less extent in the patients of the control group.

The degree of reduction of the products of peroxidation of lipids (diene conjugates and malonic dialdehyde) in the course of the dietotherapy with the use of the proposed food additive was twice as high in the patients of the experimental group comparing with the control. A marked antioxidant effect of the nutraceutic under trial might be, in particular, due to the presence of some microelements therein, which possess an antiperoxidant action, such as chromium.

Use of the proposed food additive as part of the antiatherosclerosis diet was found to produce a definite immunomodulating effect. As seen from Table 6, no perceptible changes in the system of humoral immunity were observed in the patients of the control group given the basis diet. On the other hand, enriching the Ar diet

with the proposed food additive contributed to a reliable increase in the blood concentration of immunoglobulins A and G.

Table 4

5 Changes in the clinicobiochemical characteristics resultant from the effect of the administration of the proposed food additive concurrently with the Ar diet in the patients with hypertensive disease and concomitant adiposity

10	Character-istics	Experimental group		Control group	
		before treatment	after treatment	before treatment	after treatment
		2	3	4	5
15	Cholesterol, mmole/l	6.59+0.17	5.49+0.18*	6.11+0.22	5.50+0.26
	Tri-glycerides, mmole/l	1.37+0.14	1.48+0.13	1.81+0.26	1.42+0.18
20	Glucose, mmole/l	6.66+1.4	6.17+0.85	6.23+2.11	5.64+0.95
	Total				

	1	2	3	4	5
protein,					
g/l	81.9+2.58	77.8+2.94	79.2+5.83	76.0+4.39	
Uric acid,					
5 mmole/l	252+90	261+94	320+63	255+52	
Bilirubin,					
mmole/l	14.3+1.43	9.88+0.88	24.2+3.51	19.9+2.11	
AST, IU/l	24.6+3.39	17.8+1.64	26.5+3.24	22.8+3.22	
ALT, IU/l	15.6+4.20	17.7+4.78	39.4+4.25	31.5+3.97	
10 Creatinine,					
mmole/l	64.9+3.39	70.4+3.61	59.7+4.96	62.4+3.55	
Urea,					
mmole/l	6.98+0.29	4.91+0.34	6.63+0.34	5.64+0.29	
Albumin,					
15 g/l	44.9+0.48	44.3+0.62	43.1+0.29	42.7+0.35	
Globulin,					
g/l	36.8+1.34	33.4+1.48	36.5+0.32	34.2+0.33	
Calcium,					
mmole/l	2.48+0.37	2.48+0.29	2.52+0.24	2.49+0.25	
20 Phosphorus,					
mmole/l	0.74+0.05	0.92+0.06	0.88+0.05	0.87+0.07	
Prothrombin,					
%	98.1+2.11	90.7+0.99	92.0+4.92	84.3+2.72	
Fibrinogen,					
25 mg %	343.0+23	372.5+27	371.2+45	322+42	

1	2	3	4	5
Fibrinolysis				
time, min	268.9+14.2	216.7+12.5	196.4+26.1	187.5+29

Note. * - with $p < 0.05$.

5

Table 5

Changes in the characteristics of the system "peroxidation of lipids - antioxidant protection" under the effect of the proposed food additive concurrently with Ar diet in the patients with hypertensive disease and concomitant adiposity

Character- istics	Experimental group		Control group	
	before treatment	after treatment	before treatment	after treatment
15	1	2	3	4
				5

Glutathione

reductase,

mmole

NADPH/min/ml

20 erythr. 2.78+0.12 2.45+0.06 2.28+0.04 2.36+0.12

	1	2	3	4	5
Glutathione peroxidase, mcmole 5 NADPH/min/ml					
erythr.	35.4+0.27	48.2+0.14	32.4+0.29	35.0+0.15	
Catalase, kU/ml					
erythr.	261+16.2	244+10.0	290+7.3	297+10.2	
10 Superoxide dismutase, AU/ml					
erythr.	2347+53	3741+60	2487+74	2706+81	
Vitamin A, 15 sera, mg %	14.3+1.05	18.8+0.94	15.7+0.83	16.2+1.12	
Vitamin E, sera, mg %	0.73+0.04	0.97+0.05	0.80+0.03	0.82+0.06	
Vitamin C, sera, mg %	0.60+0.01	0.88+0.02	0.68+0.03	0.74+0.04	
20 SH-groups, sera, mmole/l	2.56+0.09	2.78+0.11	2.38+0.11	2.48+0.07	
Malonic dialdehyde, 25 mmole/ml	3.84+0.06	2.50+0.08*	3.68+0.09	3.07+0.12	

	1	2	3	4	5
Diene conjugates, nmole/ml					
5 erythr.	3.58+0.10	2.32+0.06	3.27+0.14	2.69+0.12	

Table 6

Changes in the characteristics of humoral immunity under the effect of the proposed food additive concurrently with Ar diet in the patients with hypertensive disease and concomitant adiposity

	Character- istics, mg/100 ml	Experimental group		Control group	
		before treatment	after treatment	before treatment	after treatment
15	1	2	3	4	5
	Immuno- globulin A	247+14	336+18'	278+20	303+14
	Immuno- globulin G	905+53	1234+61	947+54	912+60
20	Immuno- globulin M	257+12	278+14	236+10	241+12

	1	2	3	4	5
Complement					
C3					
component	90.7+3.6	89.0+2.1	95.4+4.0	92.3+1.7	
5 Complement					
C4					
component	28.4+1.06	26.3+1.34	25.7+0.94	27.4+0.76	

* - $p < 0.05$

Thus, in-depth chemical studies and extensive
 10 preclinical trials have demonstrated that ossified deer
 antlers are a natural accumulator of valuable useful
 chemical elements and biologically potent components
 that have been maturing for 7-8 months.

That is why to use deer antlers in the stage of
 15 their development, that is, antlers of young deer,
 implies producing medicinal preparations (pantocrine,
 rantarine) and food additives from an immature product
 which is more toxic and less efficient.

The herein-proposed powdery biogenic preparation
 20 from ossified deer antlers and the food additive based
 on said preparation having the characteristics as
 specified by the present invention, provide for
 administering to human organism the product retaining by
 100% its natural composition.

WHAT WE CLAIM IS:

1. A powdery biogenic preparation from ossified deer antlers, consisting of porous particles of a disintegrated initial product, the dispersity of said particles being largely below 0.25 mm, their specific surface about 100 sq.m/g, and a pore volume of about 3.0 cu.m/g.

2. A powdery biogenic preparation as set forth in claim 1, containing principally the following components:

	lipids	0.13-0.25 wt.%
	essential amino acids and peptides,	
	not less than	0.80 mg/g
	cholesterol	0.10-0.20 mg/g
15	phosphorus, not less than	3.5 wt.%
	calcium	15.0-20.0 wt.%
	iodine	0.02-0.04 wt.%
	magnesium, not more than	6800 mcg/g
	barium, not more than	31.30 mcg/g
20	manganese, nor more than	3.5 mcg/g
	tin	0.50 mcg/g
	copper	0.5-20.0 mcg/g
	iron	60-240 mcg/g
	zinc	60-120 mcg/g
25	lead, less than	0.35 mcg/g
	cadmium, less than	0.001mcg/g
	cesium	4-12 mcg/g

strontium	5-10	mcg/g
potassium	300-600	mcg/g.

3. A food additive, comprising a powdery biogenic preparation from ossified deer antlers, the porous particles of said preparation featuring a dispersity principally below 0.25 mm, a specific surface of about 100 sq.m/g, and a pore volume of about 3.0 cu.m/g.

4. A food additive, wherein said biogenic preparation contains the following components:

10	lipids	0.13-0.25 wt.%
	essential amino acids and peptides,	
	not less than	0.80 mg/g
	cholesterol	0.10-0.20 mg/g
	phosphorus, not less than	3.5 wt.%
15	calcium	15.0-20.0 wt.%
	iodine	0.02-0.04 wt.%
	magnesium, not more than	6800 mcg/g
	barium, not more than	31.30 mcg/g
	manganese, nor more than	3.5 mcg/g
20	tin	0.50 mcg/g
	copper	0.5-20.0 mcg/g
	iron	60-240 mcg/g
	zinc	60-120 mcg/g
	lead, less than	0.35 mcg/g
25	cadmium, less tha	0.001mcg/g
	cesium	4-12 mcg/g
	strontium	5-10 mcg/g
	potassium	300-600 mcg/g.

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